Pathway Analysis of the Movement of Recovered Cattle From a FMD-Infected Feedlot to Slaughter

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List of Figures

List of Tables

Abbreviations

APHIS	Animal and Plant Health Inspection Service
FMD	Foot and Mouth Disease
FMDv	Foot and Mouth Disease virus
FSIS	Food Safety Inspection Service
NAHEMS	National Animal Health Emergency Management System
OIE	World Organization for Animal Health, Office International des Epizootics
OP	Oesophageal-pharyngeal
US	United States of America
U.S.C.	United States Code
USDA	United States Department of Agriculture
USDA ERS	United States Department of Agriculture Economic Research Service
USDA FAD PReP	United States Department of Agriculture Foreign Animal Disease Preparedness and Response Plan
USDA NASS	United States Department of Agriculture National Agricultural Statistics Service
VI	Virus isolation

Definitions

Actively Infected premises: Premises where a presumptive FMD positive case or confirmed positive case exists based on laboratory results, compatible clinical signs, case definition, and international standards.

Aerosol transmission: The introduction of airborne droplet nuclei or small particles in the respirable size range containing infectious agents into the air.

At-risk premises: Premises with susceptible animals that have not developed clinical signs compatible with FMD.

Backgrounding or Stocker Operation: A stage of cattle production when calves eat roughage and/or light energy rations or graze pasture (native grass or winter wheat), which encourages structural growth. During the backgrounding period, producers decide when to place them in feedlots to fatten for slaughter.

Beef replacement heifer: A young female bovine that is raised for the purpose of replacing and improving the cow herd.

Carrier cattle: Cattle that have recovered from clinical disease and have at least one of multiple positive oesophageal-pharyngeal samples 28 days post infection with FMDv (as defined by OIE).

Clinically-infected/Clinically infectious phase (Ic): Animal is viremic, shedding virus and is exhibiting clinical signs of disease.

Confirmed positive case (of FMD): An animal with clinical signs consistent with FMD and from which FMDv is isolated and identified in a USDA laboratory or other laboratory designated by the Secretary of Agriculture.

Control Area: Consists of an infected zone and a buffer zone. Initially, the entire State, Commonwealth, Tribal Nation, or territory may be declared a control area and subject to movement restrictions until appropriate surveillance and epidemiological evidence has been evaluated and the extent of the outbreak known.

Cow-Calf Operation: An operation that breeds and maintains cows for the primary purpose of producing calves to enter the beef production system.

Cross-contamination: The transfer of harmful bacteria, viruses or other microorganisms from an infectious animal or site to a susceptible animal or site either directly, or indirectly via a fomite.

Environmental Contamination: The introduction of infectious organisms into water or soil from excretions or secretions of infected animals.

Environmental Fomites: Dirt, dust, bedding, manure, and urine particles that are capable of carrying infectious organisms and transfer them to susceptible animals.

Excretions: Waste matter that has been expelled from animals (i.e. manure, urine, sweat)

Feedlot (feedyard): An operation or facility (premises) where cattle are fed in a confinement setting primarily for the purpose of harvesting for beef production. Cattle are kept in groups/pens and fed custom diets that are designed for efficient weight gain. Cattle enter

feedlots as weaned calves from cow-calf operations, stocker or yearling cattle that have been backgrounded at stocker operations and may range in weight from 350 – 1000 lbs. Cattle leave the feedlot when they have reached target market weights ranging from 1200 – 1600 lbs.

Feeder cattle: Calves primarily from cow-calf operations that are marketed to be placed into a feedlot to be fed primarily for the production of beef.

Fomites: Inanimate objects (i.e. equipment, vehicle) that, when contaminated with a viable disease agent, can serve as a source of infection for a susceptible host (i.e. equipment, vehicle).

Free Country or Zone: OIE defines a country or zone to be FMD-free by stamping out without vaccination after minimum of 3 months. If a country or zone uses vaccination, this waiting period becomes 6 months. If the "vaccination-to-live plan" is used without stamping out, these waiting periods become 1 year and 2 years, respectively. This definition is based on the assumption that "free" means no infectious animals are present.

Hazardous Material: A substance or material that the Secretary of Transportation has determined is capable of posing an unreasonable risk to health, safety, and property when transported in commerce in a particular amount and form, and has been designated as hazardous under section 5103 of federal hazardous materials transportation law (49 U.S.C. 5103). The term includes hazardous substances, hazardous wastes, marine pollutants, elevated temperature materials, materials designated as hazardous in the Hazardous Materials Table of 49 CFR 172.101, materials that meet the defining criteria for hazard classes and divisions in part 173 of subchapter C of chapter I.

Herd: The population of animals at defined premises.

ID_{50}: Infectious Dose 50; amount of pathogen measured as number of colony forming units (CFU) for bacteria or number of virus particles required to infect 50% of exposed individuals.

Incubation Period: The known or assumed period between the introduction of a pathogen into a susceptible animal and the occurrence of the first clinical signs of the disease.

Infected: Includes all phases of disease (L + Ip + Ic): latent (L), pre-clinically infected (Ip) and clinically infected (Ic).

Latent phase (L): Susceptible animal has been exposed and is incubating the virus, but is not viremic.

Mechanical Transmission: The passive transfer of harmful agents of disease, either indirectly via fomites or directly via vectors.

Non-carrier cattle: Cattle that have recovered from clinical disease, no longer harbor FMDv and, therefore, are no longer infectious.

Operations: Farm, ranch, feedlot, or other organized unit of production.

Pre-clinically infected phase/Pre-clinically infectious: Animal is viremic, is shedding virus, but has not yet developed clinical signs. Pre-clinical animals also fall into the viremic non-clinical group.

Premises: Locations where livestock are raised, housed, or pass through during commerce.

Pre-viremia: The period from which an animal is first infected with FMDv until virus is first detected within circulating blood with a sustained and increasing trend. This period includes the latent phase (Arzt, Juleff, Zhang, & Rodriguez, 2011).

Post-viremia: The period following viremia and it begins with the first negative blood assay. This period includes: resolution of clinical signs, persistent infection, and chronic phase (Arzt et al., 2011).

Probang (oesophageal-pharyngeal) samples: These samples are collected by inserting a probang (a slender rod with a sponge or ball at the end) over the tongue and moving it vigorously back and forth between the first part of the esophagus and the back of the pharynx.

Recovered phase (R): Previously infected animal where at least 28 days have passed since the last observable clinical signs (OIE).

Recovered premise: A premise previously infected with FMD where at least 28 days have passed since the last observable clinical signs. This definition is based on the assumption that all cattle on the premise have recovered from clinical disease, resulting in a population that contains only recovered cattle that are either carriers or non-carriers. This definition is in contrast to the OIE definition of a Free Country or Zone (see above for definition).

Secretions: Substances that are released from a gland or cell (i.e. nasal fluids, respiratory fluids, ocular fluids).

Shedding phase: Time interval between the time an animal begins shedding virus to the time an animal is no longer shedding virus and it includes the pre-clinical, and clinical infectious phases.

Slaughter/Harvest establishment: Premises that receive cattle for slaughter that may be located within or outside of the control area.

Stamping out: Depopulation of clinically affected and all presumed exposed susceptible animals located on a premise.

Sub-clinical animals: Infection of animals with FMDv where that event is never followed by observable signs of clinical disease. Animals are considered to be infectious and represent a risk for spread of the virus because they can go undetected. Sub-clinical animals also fall into the viremic non-clinical group.

Susceptible: Healthy animal species that have the potential to become infected with FMDv.

$TCID_{50}$: Tissue Culture Infective Dose 50; the amount of a pathogen measured as number of virus particles required to produce pathological change in 50% of cell cultures inoculated, expressed as $TCID_{50}$/ml.

Vector: An organism that does not cause disease, but spreads infection by moving the pathogens between hosts.

Viremia: FMDv is circulating in the blood stream and there is evidence of active viral replication. Susceptible species can be viremic and shedding virus before they develop clinical

signs. Includes the pre-clinical (I) and clinical (C) phases of the disease in this pathway analysis. Onset of viremia has been found to occur 16-72 hours post-inoculation (Arzt et al., 2011).

Viremic non-clinical animals: Animals that are not showing clinical signs but are shedding the virus. This group includes animals that are both pre-clinical and sub-clinical.

Weaned calf crop: The number of calves birthed on a cow-calf operation that go on to be weaned.

Executive Summary

The present document proactively evaluated the FMDv transmission pathways associated with the movement of beef cattle not showing Foot and Mouth Disease (FMD) clinical signs from recovered or infected feedlot premises to offsite harvest facilities during a FMD outbreak. The analysis evaluated the most up to date available science and solicited opinion from experts when data was lacking. This analysis was proactive in nature and the scenarios, pathways and conveyance types assessed were based on the current practices and regulations applicable during a FMD outbreak in the United States (US). Modeling was used to estimate the number of latent, pre-clinical, clinical, and recovered animals during the course of infection at various time intervals. The main outcomes of the analysis should be reviewed if needed as new data becomes available in the future.

Main results:

"Stamping out" FMDv infected premises has, historically, been the method of choice in the control of FMDv outbreaks. The purpose of this pathway analysis was to provide insight into the potential pathways for viral spread associated with alternative solutions to stamping out in the event of a catastrophic FMDv outbreak in the U.S.

Modeling results are based on the assumption that FMD detection would occur when 10% of a 10,000 head herd is showing clinical signs, which was predicted to occur at approximately 17.5 days (95% Confidence Interval: 17.4-17.7) post-infection. At this time, the percentage of viremic pre-clinical and clinical animals that are actively shedding virus would be approximately 11% (1,095/10,000) and 7% (692/10,000), respectively. If a decision is made to move animals not showing clinical signs at this point, a significant proportion of pre-clinical animals will be part of the group moving to harvest.

The pathway analysis identified the following variables associated with the likelihood of disease transmission during the movement of cattle from infected or recovered feedlot premises:

Mechanism of spread:

Samples taken from infected animals that had the highest FMDv concentration were nasal discharge (6.09 log $TCID_{50}$/mL), upper respiratory tract (5.70 log $TCID_{50}$/mL), skin (7.4 log $TCID_{50}$/mL), and probang samples (4.91 log $TCID_{50}$/mL). Airborne excretion (4.33 log $TCID_{50}$/mL) of virus also represents route of virus transmission. The bodily secretions/excretions with the lowest FMDv amount were urine (1.93 log $TCID_{50}$/mL) and manure (1.55 log $TCID_{50}$/mL). While urine and manure were shown to carry the least amount of virus, these excretions are likely to be present in significantly higher amounts in the environment and, consequently, on the

animals and within the truck during transport. It is, therefore, important to consider how the amount of each secretion/excretion could contribute to disease spread.

Disease phase:

Transmission more likely: Viremic non-clinical (pre-clinical and sub-clinical) animals are more likely to transmit disease. Model results showed a waiting period of 25 days post-detection (assuming detection occurred on day 17 post-infection) would reduce the proportion of viremic pre-clinical animals to almost 0 (1.2/10,000) and actively shedding animals to 1.9% (189/10,000). In this scenario, most of the animals would be recovered from clinical infection.

Transmission less likely: Non-viremic, non-clinical (latent or recovered) animals are less likely to transmit disease. While virus has been found to be present in animals during these phases, there has been no evidence of transmission.

Time of movement:

Transmission more likely: Disease transmission is more likely to occur when high numbers of viremic animals are present. This would result in increased shedding during transport and increased virus in the farm environment. Model results showed the highest number of viremic pre-clinical and clinical animals to be present around 11 days post-detection (assuming detection occurred on day 17 post-infection), with proportions of 5.1% (512/10,000) and 28.5%(2,851/10,000), respectively.

Transmission less likely: Disease transmission is less likely to occur when low numbers of viremic animals are present. Model results showed a waiting period of 48 days post-detection would result in the lowest number possible of pre-viremic and clinical animals at 0.00002% (0.002/10,000) and 0.009%(0.94/10,000), respectively. At this point, approximately 96% (9,628/10,000) of the herd is recovered from clinical infection and, therefore, less likely to transmit the disease.

Vaccination status:

Transmission more likely: The group that is more likely to transmit disease would be those animals that are not vaccinated since vaccination has been shown to greatly reduce the amount of viral shedding and clinical signs.

Transmission less likely: The group that is less likely to transmit disease would be those animals that are vaccinated. The efficacy of the vaccine would be partially dependent on the time that has elapsed between immunization and disease exposure as vaccines have been shown to be more effective when time is allowed for the animal to develop immunity prior to exposure.

The document identified several data gaps and further research is recommended to better estimate the risk of disease spread associated with each pathway and to be able to provide recommendations for the movement of cattle in these scenarios.

Background

This pathway analysis was performed by the University of Minnesota's Center for Animal Health and Food Safety to proactively evaluate different scenarios for moving beef cattle from a FMD-infected or FMD-recovered feedlot premises during a FMD outbreak in the US to slaughter, as it relates to potential spread to susceptible livestock.

FMD is a highly contagious viral disease of cattle and other cloven-hoofed animals such as swine, sheep, and goats. Thus, there is great potential for this virus to cause severe economic loss when animals become affected. Infection with the virus is characterized by fever and blister-like sores on the feet, tongue, lips, inside the mouth and in females on the teats, resulting in weakened animals and, ultimately, reduced production.

In the event of a FMD outbreak in the US, Local, State and Federal authorities will implement a foreign animal disease emergency response as described in the United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) Framework for Foreign Animal Disease Preparedness and Response Plan (USDA APHIS, 2014). This response includes control and eradication strategies that will utilize depopulation, quarantine, vaccination, and movement control measures to stop the virus spread and eliminate it from affected and susceptible populations. For the purpose of this analysis, knowledge of how authorities will respond to a catastrophic FMD outbreak will be as follows:

- Transition to a long-term eradication program, including *Emergency Vaccination to Live without Stamping-Out:* Vaccination of susceptible animals without depopulation of infected animals or subsequent depopulation of slaughter or vaccinated animals (USDA APHIS, 2014). This strategy involves the following:
    - A protective emergency vaccination strategy
    - Requires the establishment of one or more Vaccination Zones (VZ) free of FMD, the establishment of one or more Control Areas (CA) for infected animals, and movement controls to keep infected animals out of VZs free of FMD.
    - DIVA (Differentiating Infected from Vaccinated Animals) testing may be necessary for movement between zones, interstate commerce, and international trade.
    - Vaccinated animal identification, movement controls, traceability, and an effective, scalable permitting system may be necessary.
- Transition to allowing movement of vaccinated animals (14 days post-vaccination) from premises with no current clinical evidence of infection with Foot and Mouth Disease virus (FMDv).

- Consideration will be given to allowing movement of non-infected animals (including vaccinated animals) according to the Secure Food Supply Plans. Animals must meet vaccination withdrawal period (if it applies) and be able to pass Food Safety Inspection Service (FSIS) ante-mortem inspection to be slaughtered.

A pathway analysis in the animal health context comprises a framework that identifies the potential routes of spread of a pathogen or virus in a country, region or farm using available scientific information. Completing this type of analysis in a timely manner during an outbreak is typically impractical. Analyses conducted proactively, before an outbreak occurs, provide the framework necessary for decision makers to identify and better understand the different risks associated with the movement of live animals. This pathway analysis is a component of a full risk assessment and the risk assessment process will more fully evaluate the risks that were identified in the different pathways.

The literature and expert opinions used to guide this document were based primarily on experimental work in which a limited number of animals and specific virus strains were analyzed. This document should not be used to predict the spread of disease in an outbreak as actual virus behavior in an outbreak could vary significantly depending on the circumstances.

Scope

The purpose of this document is to provide a pathway analysis for the movement of beef cattle not showing FMD clinical signs from FMD-infected and FMD-recovered feedlots to slaughter within or outside of the control zone in the event of a FMD outbreak in the U.S. The analysis is based on the potential presence of infectious FMDv in the live cattle or on fomites at the time of transportation and the potential release of the virus with the movement of live cattle to slaughter. The analysis discusses the opportunities that: 1) Vaccinated and unvaccinated cattle with potential for spreading the virus (latent, viremic non-clinical, or carrier) could be moved from the infected/recovered premises to the harvest site; 2) Infectious FMDv could be present in the animals moved to slaughter and/or on fomites and released into the environment during transportation.

A 42 day post-detection waiting period was chosen in two of the scenarios based on an estimate of the total time it would take for an individual animal to enter the recovered phase. This number was established based on knowledge of the following:

- A clinically infectious phase that lasts up to 14 days.
- The OIE definition of recovered which states, "a previously infected animal where at least 28 days have passed since the last observable clinical signs".

The sum of these two numbers means that 42 days after detection, you can assume an infected animal has most likely entered the recovered phase.

This analysis utilizes five possible scenarios to represent potential situations at the time of transportation of live cattle from a feedlot (assuming all animals to be moved are free from clinical signs of FMD):

1. The disease is allowed to progress through an infected herd and at least 42 days have passed since the first observable clinical signs in the herd prior to movement of eligible cattle (at or near target weights) to harvest.
2. The feedlot is actively infected (animals with clinical signs are present) and cattle not showing clinical signs of FMD (non-infected, latent, viremic non-clinical, recovered) that are eligible for harvest (at or near target weights) are moved to harvest.
3. Upon detection, all cattle in the infected feedlot are vaccinated, at least 42 days have passed since the first observable clinical signs and cattle eligible for harvest (at or near target weights) are subsequently moved to harvest.
4. Upon detection, all cattle in the infected feedlot are vaccinated, at least 14 days have passed as the waiting period and cattle not showing clinical signs of FMD (non-infected, latent, viremic non-clinical, recovered) that are eligible for harvest (at or near target weights) are moved to harvest.

5. The feedlot is not known to be infected (infected but undetected or negative) and located within a control zone. All animals have been vaccinated and cattle eligible for harvest (at or near target weights) are moved to harvest after the 14 day waiting period.

Assumptions

This pathway analysis takes into consideration all applicable regulations, including preventive measures already in place, as well as additional preventive measures that will likely be implemented during an outbreak based on current USDA policy. This analysis is proactive in nature and cannot address the specific circumstances surrounding an outbreak in detail. Therefore, some assumptions were made to establish context and applicability. These assumptions are:

- There is an ongoing FMD outbreak in the U.S.
- Response is following the USDA FMD response plan, quarantine and movement control.
- The FMD outbreak is at a scale (Type 4: Widespread or National FMD Outbreak or Type 5: Catastrophic FMD Outbreak) that has become endemic and strategies besides depopulation, proposed by the FAD PReP Strategy Document, vaccinate-to-live and vaccinate-to-slaughter, are being considered.
- The outbreak is caused by a single type of FMDv.
- Animals showing clinical signs will not be moved from the premise.
- The infected premise is a large scale feedlot (> 10,000 head).
- Biosecurity measures were implemented at affected farms and followed the National Animal Health Emergency Management System (NAHEMS) Guidelines.
- All transport methods/vehicles will be cleaned and disinfected after each load and unload of cattle following FAD PRep guidelines.
- The analysis will consider the pathways associated with the movement of cattle from feedlot premises to harvest only; movements to other types of facilities are not considered.

Hazard identification

Background

FMD is a highly contagious viral disease affecting primarily cloven-hoofed animals. The disease is characterized by the development of vesicles in and around the mouth and on the feet. Although natural FMD infection rarely causes death of mature animals, the disease results in decreases in livestock productivity and causes serious economic impacts on international trade of animals and animal products (OIE, 2013).

FMD was last reported in the U.S. in 1929 and in North America in 1952 (Canada) and 1954 (Mexico). As of November 2015, of the OIE's 180 Member Countries, 67 are recognizes as free without vaccination. The OIE recognizes 1 country as free with vaccination and 16 have official free zones (12 without vaccination, 8 with vaccination). The United States recognizes 3 countries that have FMD-free zones without vaccination and does not recognize zones or countries as FMD-free with vaccination (USDA APHIS, 2015). The potential risks and impacts that FMD may pose were demonstrated by the severe economic and livestock losses experienced in the United Kingdom in 2001 and the consequences of these FMD outbreaks have reinforced the need for FMD awareness and evaluation of the possible pathways by which FMDv can spread.

Virus Characteristics

There are seven FMDv serotypes: A, O, C, SAT (South African Territories) 1, 2, 3, and Asia 1. Each serotype can be divided further into subtypes. Within each serotype is a spectrum of antigenic variation, resulting in strains having close or distant relationships to each other. All serotypes produce disease that is clinically indistinguishable, but immunologically distinct. No cross-immunity is conferred between serotypes. Serotype O is the most common serotype isolated from the field and occurs in many parts of the world and serotype A is considered to have the greatest antigenic variation (Alexandersen & Mowat, 2005; Jamal & Belsham, 2013; Kitching, Knowles, Samuel, & Donaldson, 1989; Knowles & Samuel, 2003).

Host range of FMD

Cloven-hoofed animals (ungulates) are the natural domestic and wild hosts of FMDv. They are susceptible to all 7 serotypes and many of the subtypes of FMDv. The severity of illness may differ depending on the specific serotype and the species that is affected. Susceptible species include, cattle, pigs, sheep, goats, water buffalo, impala, bison, African buffalo, American bison, antelope, reindeer, moose, elk (although low), hedgehogs, porcupines, giraffes, elephants and Bactrian camels. Water buffalo and African buffalo are of particular importance because of their ability to act as carriers and maintain the virus for long periods of time. Horses are resistant to FMD infection and New World camelids (llamas, alpacas, vicunas and guanacos)

have low susceptibility to FMD infection. FMDv may also be transmitted to mice, rats, guinea-pigs, rabbits, hamsters, embryonating chicken eggs, chickens, and various wild species, including European hedgehogs, chinchillas, muskrats, armadillos and peccaries. However, these latter species are not generally capable of spreading FMD (Alexandersen & Mowat, 2005).

Humans can become infected with FMD through (1) handling of diseased livestock with virus entry through skin wounds and mucous membranes, (2) exposure through laboratory situations, or (3) by drinking infected raw milk. The virus is not readily transmissible to humans and thus, should not be considered a zoonotic disease. Cases of human disease are rare and have resulted in temporary and mild signs of disease (fever, vesicles on the hands, feet or in the mouth) (Alexandersen & Mowat, 2005).

Environmental Persistence

FMDv retains infectivity for considerable periods of time in the environment, provided it is protected from desiccation, heat and adverse pH conditions. Various studies suggest FMDv remains viable for a wide range of times based on fomites and environmental conditions (The Center for Food Security and Public Health - Iowa State University, 2014). The virus may survive for 14 days in dry fecal material; six months in slurry in winter; 39 days in urine; 28 days on the surface of soil in autumn; and three days on the surface of soil in summer. Such observations have generally been made in countries with a temperate climate, and these survival times can be expected to be similar in hotter climates (Geering WA., 2002). In the lab, FMDv has been shown to survive more than 3 months on bran and hay, about 2 months on wool at 4°C, and 2 to 3 months in bovine feces (The Center for Food Security and Public Health - Iowa State University, 2014). FMDv is sensitive to desiccation. Relative humidity and temperature are the primary factors that affect survival of the virus in the environment. The virus survives best when the relative humidity exceeds 70%, and has poor survival when the relative humidity is below 50-60% (Sellers, 1971) but this can vary depending on the FMDv strain that is circulating. Virus stability increases at lower temperatures and has been shown to remain viable for up to one year at 4°C in cell culture medium (The Center for Food Security and Public Health - Iowa State University, 2014). FMDv is inactivated when the pH is below 6.0 or above 9.0 (OIE, 2013; The Center for Food Security and Public Health - Iowa State University, 2014). Sunlight and ultraviolet radiation have little effect on virus persistence (Donaldson & Ferris, 1975). These data support the potential risk for disease transmission to susceptible species due to the FMDv survival in truck surfaces and fecal material during the movement of infected animals to the harvest facility.

Transmission

Mechanism of Spread:

FMDv is highly contagious, and can be transmitted by a variety of mechanisms. The most common mechanism of spread of FMDv is by direct animal contact, which can occur by the airborne transfer of droplets or by mechanical transfer through cuts or abrasions in the skin or mucous membranes. Other common mechanisms by which FMDv is spread are summarized below (Alexandersen, Zhang, Donaldson, & Garland, 2003; Alexandersen & Mowat, 2005; Gloster et al., 2010).

- Indirect mechanical transfer through susceptible animal contact with virus on the surfaces of fomites (hands, footwear, clothing, vehicles, and equipment) and subsequent virus entry through cuts or abrasions in the skin or mucosa.
- Ingestion of FMDv contaminated feed or contact with contaminated animal products (milk, meat, semen).
- Spread by wind, which requires the simultaneous occurrence of particular epidemiological and climatic conditions. This type of spread will have a more significant effect on cattle and other ruminants as they have been shown to be more sensitive to infection by the airborne route.

Virus Infectivity in Cattle:

Cattle have been shown to require as little as 10 to 25 $TCID_{50}$ (tissue culture infective dose) of virus to establish infection via the respiratory route (Donaldson, Gibson, Oliver, Hamblin, & Kitching, 1987; Kitching, Hutber, & Thrusfield, 2005; Thurmond & Perez, 2006) due to their large respiratory volume. Cattle require a higher dose via the oral route and this has been shown to be 10^5 to 10^6 $TCID_{50}$ (Alexandersen et al., 2003; Sellers, 1971). Nasal instillation also requires a much larger volume than the respiratory route at 10^4 to 10^5 $TCID_{50}$ (Alexandersen et al., 2003; McVicar & Sutmoller, 1976). The dose to establish infection via damaged skin required as low as 100 $TCID_{50}$, although more consistent results were observed closer to a dose of 10^4 to 10^5 $TCID_{50}$ (Alexandersen et al., 2003; Sellers, 1971). The data is displayed in Table 1. These doses represent estimates based on experiments of small groups of animals and they may not be applicable to a large herd.

Table 1: Estimated minimum FMDv doses for infection in cattle (Alexandersen et al., 2003)

	Inhalation	Intradermal	Intramuscular	Nasal Instillation	Oral	Units
Cattle	10	100	10^4	$10^4 – 10^5$	10^5 - 10^6	$TCID_{50}$

Incubation Period

The incubation period of an infectious disease is the time interval between exposure to an infective dose and development of clinical signs and it includes both the latent and pre-clinical infection phases. The incubation period for FMD is known to be variable and dependent on the

strain and dose of the virus, the route of transmission, the husbandry situation, and the species (Alexandersen et al., 2003; Alexandersen, Kitching, Mansley, & Donaldson, 2003; Alexandersen, Quan, Murphy, Knight, & Zhang, 2003; Alexandersen & Mowat, 2005). It is well-known that FMD infected animals can shed virus during the pre-clinical infectious phase of the incubation period, before the first detectable clinical signs are noted (Mardones, Perez, Sanchez, Alkhamis, & Carpenter, 2010; Orsel, Bouma, Dekker, Stegeman, & de Jong, 2009) (Figure 1).

While the incubation period has been shown to range from 2 to 14 days in cattle, the OIE uses the full 14 days as the incubation period of FMD for control purposes. This variation in time is the result of the following (Alexandersen et al., 2003; OIE, 2013):

- A strong relationship between dose and length of incubation. The higher the dose, the shorter the incubation period.
- This concept also holds true for amount of contact between animals. The more contact infected animals have with one another, the shorter the incubation period.
- Stocking density, herd management, housing, ventilation and handling all play a role in how quickly the virus will spread through the infected herd.

Disease Phases

The shedding phase of an infectious disease is the time interval between the time an animal begins shedding virus to the time an animal is no longer shedding virus and it includes the pre-clinical, and clinical infectious phases (Figure 1). The carrier phase includes animals that have recovered from clinical disease and have at least one positive oesophageal-pharyngeal sample 28 days post infection with FMDv.

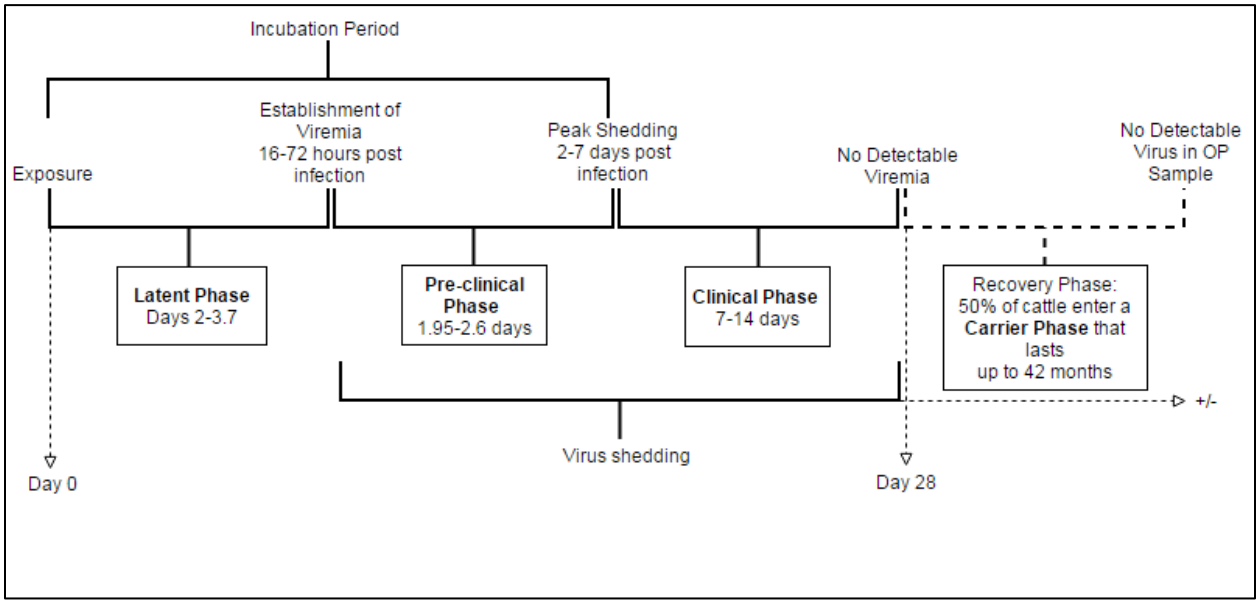


Figure 1: FMDv infection timeline by phase

Latent Phase: During this phase, virus is not detectable in the blood and animals are generally not considered to be infectious. The mean length of time this phase was shown to last in beef and dairy cows was between 2 to 3.7 days (Backer, Hagenaars, Nodelijk, & van Roermund, 2012; Bates, Thurmond, & Carpenter, 2003; Carpenter, Thurmond, & Bates, 2004; Mardones et al., 2010).

Pre-clinical phase: In this phase, the animal is viremic, is shedding virus, but has not yet developed clinical signs. Studies have shown this phase to last from 1.95 to 2.6 days (Bates et al., 2003; Carpenter et al., 2004; Mardones et al., 2010; Orsel et al., 2009). The onset of viremia has been shown to occur at or near the peak of FMDv detection from OP samples and that is at 16 to 72 hours (up to 3 days) post-inoculation (Arzt et al., 2011; McVicar & Sutmoller, 1976). While viremia typically coincides with the clinical phase of the disease, it can be readily detectable 1 to 2 days prior to the development of clinical signs (Alexandersen, Zhang, Reid, Hutchings, & Donaldson, 2002; Alexandersen et al., 2003; Arzt et al., 2011). Once the animal becomes viremic, all excretions and secretions can contain virus (Alexandersen et al., 2003; Arzt et al., 2011). There is a higher likelihood of transmission from this group because of their ability to shed virus for 1-2 days prior to showing any clinical signs of disease.

The presence of infectious virus in the oropharyngeal area can be detected as early as 2 to 14 hours after intranasal deposition (depending on viral strain and dose administration) which is well before clinical signs may appear (Arzt et al., 2011; McVicar & Sutmoller, 1976). However, the presence of infectious virus does not always mean transmission will occur as enough virus must be present in order for it to cause disease.

Sub-clinical phase: Orsel et al., 2009 described sub-clinically infected animals as those who shed virus without ever developing clinical signs (Orsel et al., 2009). This is in contrast to pre-clinical animals, in which a proportion of the animals that are shedding without showing clinical signs go on to develop clinical disease (Blanco, Romero, El Harrach, & Sanchez-Vizcaino, 2002). Studies have shown that a high proportion (11%) of susceptible cattle that were exposed by contact to a variety of strains did not develop clinical signs of FMD while they were shedding virus (Sutmoller & Casas, 2002). These animals represent a higher likelihood of disease spread because they may be shedding virus and go undetected (Sutmoller & Casas, 2002).

Clinical phase: In this phase, the animal is viremic, shedding virus and is exhibiting clinical signs of disease. Spread from the initial sites of primary replication results in infection of the lymph nodes and the bloodstream, and resultant viremia distributes the virus to all organs and tissues. Further replication of virus occurs particularly at sites where characteristic lesions of FMD

develop (Alexandersen et al., 2003; Burrows, Mann, Garland, Greig, & Goodridge, 1981; Dillon, 2011). Clinical signs typically begin around 3-4 days post-infection (Chase-Topping et al., 2013). The peak period of shedding has been shown to occur 2 to 7 days post-infection (Parthiban, Mahapatra, Gubbins, & Parida, 2015) and may coincide with the appearance of clinical signs (McVicar & Sutmoller, 1976). Cox et al., 2005 showed the highest average levels of detectable viral RNA to be between 4 and 10 days post-challenge exposure (Cox et al., 2005). FMDv is known to have a direct effect on the skin and that it acts as a major viral replication site. While the virus is known to be present when vesicles are observed, it can also be present prior to viremia and when the skin appears normal (Alexandersen et al., 2003; Brown,C.C.1992; Dillon, 2011).

Recovered cattle (non-carriers and carriers): This term refers to cattle that have recovered from clinical disease and include animals in the carrier and non-carrier stage:

a) Non-carrier cattle are no longer carrying the virus and are considered to be non-infectious and fully recovered from FMDv.
b) Carrier cattle are defined as having at least one of multiple positive oesophageal-pharyngeal samples 28 days post infection with FMDv (as defined by OIE).

It has been shown that over 50% of cattle can become carriers with this proportion ranging from 3.34% up to 80%. (Alexandersen, Zhang, & Donaldson, 2002; Cox et al., 2005; Kitching et al., 2005; Salt, Samuel, & Kitching, 1996; Sutmoller & Casas, 2002). Cattle that become carriers may have recovered from clinical disease or had been vaccinated and exposed (Arzt et al., 2011). All 7 FMDv types are capable of inducing persistent infection lasting up to 42 months (Thomson, 1996). Alexandersen et al., 2002 hypothesizes that persistence is the result of multiple factors including; a specialized target epithelial cell population in the pharynx, and specific cellular responses (Alexandersen et al., 2002). It appears that FMDv appears to persist primarily in the throat (oropharyngeal) region of carrier cattle (Parthiban ABR., et al., 2015; Stenfeldt and Belsham, 2012; Pacheco J., et al., 2015).

The rate of FMDv transmission from carriers to susceptible animals was shown to be negligible over the course of the 75 days that the animals were observed in a recent study performed by Parthiban, et al., 2015 and it was, therefore, determined that the probability of FMDv transmission from carriers would be very low (Parthiban et al., 2015). There is currently no research or outbreak data proving the capability of carrier cattle to infect other susceptible species.

FMDv concentration in cattle secretions

Viremic non-clinical -VS- clinical cattle: A review of reported maximum virus titers in various excretions and secretions of FMDv infected cattle are displayed in Table 2 and it is important to recognize that these values can vary based on serotype and strain of FMDv. The highest FMDv median amounts in cattle were shown to reside in the upper respiratory tract secretions and excretions of cattle (Bravo de Rueda, Dekker, Eble, & de Jong, 2014). Rueda et al, 2014 also developed a model to predict the amount of virus present in various secretions during the clinical and viremic non-clinical phases (pre-clinical and sub-clinical cattle). The amount of virus was estimated to be lower in all secretions and excretions of viremic non-clinical cattle, except milk when compared to the clinical phase (Bravo de Rueda et al., 2014). While the amount of virus in the body fluids of viremic non-clinical cattle appear to be less, it is still known that disease can occur in this group of animals (Orsel et al., 2009).

Tables 2 compares the amount of FMDv found to be shed by cattle in studies with predictions of the amount of FMDv shed by clinical and viremic non-clinical cattle. The secretions and excretions that tend to contain the most virus, whether in clinical or viremic non-clinical cattle are as follows: Probang, upper respiratory tract, blood, and milk. The amount of virus excreted in these various bodily fluids as well as the amount of each bodily fluid excreted/secreted by the animals is important in determining how much virus may be transported if infected, undetected animals are moved off a premise.

Table 2: FMDv virus excretion of cattle ([1]Bravo de Rueda, et al., 2014; [2]Dillon, 2011)

	[1]Maximum virus titer average (range) [2]Average virus concentration	**[1]Model Results**	
Disease phase (combined virus excretions)	Clinical: [1]4.62 (1.00,8.50) log $TCID_{50}$/mL Viremic non-clinical: [1]4.52 (0.95,8.65) log $TCID_{50}$/ml	Clinical (log $TCID_{50}$/mL)	Viremic non-clinical (log $TCID_{50}$/mL)
Blood	[1]4.03 (0.95,6.20) log $TCID_{50}$/mL	4.55	3.58
Feces	[1]1.55 (1.50,1.75) log $TCID_{50}$/mL	1.92	1.22
Milk	[1]4.48 (2.15,7.35) log $TCID_{50}$/mL	3.97	5.8
Nasal Discharge only	[1]6.09 (2.75,7.85) log $TCID_{50}$/mL	NA	NA
Probang	[1]4.91 (2.20,8.65) log $TCID_{50}$/mL	6.71	6.07
[a]Airborne excretion	[1]4.33 (3.88,5.08) log $TCID_{50}$/mL	NA	NA
Semen	[1]4.55 (2.10,6.20) log $TCID_{50}$/mL	3.24	NA

Upper Respiratory Tract (OPF swabs, saliva and nasal discharge)	[1]5.70 (1.25,8.50) log $TCID_{50}$/mL	5.27	2.76
Urine	[1]1.93 (1.00,3.80) log $TCID_{50}$/mL	2.31	NA
Skin	Clinical: [2]7.4 log $TCID_{50}$/g Viremic non-clinical: [2]5.1 log $TCID_{50}$/g	NA	NA

*$TCID_{50}$ = the infective dose which will infect 50% of cultures.

*Maximum virus titer average = the average of maximum titers over time from individual animals

*NA = Not available

[a]$TCID_{50}$ per animal per day for airborne excretion

Table 3 summarizes the amount of FMDv that may be shed in secretions from cattle during the acute phase of the infection. These animals were followed to see if they became carriers or non-carriers following the acute phase of infection which allowed for retrospective analysis of viral shedding. Following clinical infection, approximately 50% of the animals will fully recover, meaning no virus will be present, and 50% of the animals will continue to harbor virus intermittently in the oropharyngeal region for up to 3.5 years as carriers. Parthiban et al., 2015 discusses the amount of virus shedding that will occur in clinical animals during the acute phase of the infection. Cattle that eventually become non-carriers were shown to shed less virus in both nasal fluid and saliva than cattle that became carriers. Results showed that there was variability in the amount of virus shed by animals in the acute phase of the infection and this variability is important in determining the amount of virus shedding that may be expected in an affected herd.

Table 3: FMDv concentration in the excretions/secretions of cattle during the acute phase of infection (Parthiban, et al., 2015)

		Carriers	Non-carriers	Units
Peak Shedding	Nasal Fluid	$10^{6.0}$	$10^{5.5}$	log_{10} copy number/mL
	Saliva	$10^{6.9}$	$10^{6.5}$	log_{10} copy number/mL
Total Shedding	Nasal Fluid	$10^{6.6}$	$10^{6.0}$	log_{10} area under the curve (copies/mL)
	Saliva	$10^{7.4}$	$10^{7.0}$	log_{10} area under the curve (copies/mL)

*Copy number/mL = the number of RNA copies of virus that are present in a mL.

Effects of vaccination on disease status in affected cattle

Emergency vaccination:

Emergency vaccination can be used in two different ways during an outbreak: Suppressive vaccination is used "to reduce the potential FMDv production in herds that may already have been exposed to infection, but in which very few animals are incubating disease". Protective vaccination is typically used for herds that "are in the vicinity of an outbreak but are thought not to have been exposed to live virus" (Kahn et al., 2002). In both situations, the animals that are being vaccinated are those which have not shown clinical signs of infection. Early induction of protective immunity and the use of a broad antigenic spectrum are the two most important properties of an emergency FMD vaccine (Cox, Barnett, Dani, & Salt, 1999). Studies show that if animals are sufficiently and adequately immunized by vaccination, within-herd transmission will decrease which, in turn, will decrease the likelihood of between-herd transmission (Orsel, de Jong, Bouma, Stegeman, & Dekker, 2007; Orsel & Bouma, 2009; Paton, Fussel, Vosloo, Dekker, & De Clercq, 2014). Emergency vaccination with high-potency vaccines against foot-and-mouth disease has been shown to be highly effective in preventing clinical signs in animals when the correct type and strain are used in the vaccines and when it was administered no less than 4 days prior to challenge (Barnett & Carabin, 2002; Cox et al., 2005; Doel, Williams, & Barnett, 1994; Porphyre, Auty, Tildesley, Gunn, & Woolhouse, 2013).

Effects of vaccination on cattle prior to or after exposure to FMDv:

Studies show that live virus cannot be readily isolated from animals that have undergone emergency vaccination and because of this, the likelihood of transmission to susceptible animals is low (Cox et al., 2005). While vaccinated animals appear to be protected from clinical infection, sub-clinical infection may still be present, but the level of viral replication in these animals has been shown to be "greatly reduced" (Cox et al., 2005; Cox et al., 2007)(). It is important, for the purpose of this document, to note that vaccinated animals have been shown to become sub-clinically infected if exposed to a sufficient viral challenge and also that vaccinated ruminants have been shown to develop the FMD carrier state (Barnett & Carabin, 2002; Cox et al., 2006; Paton et al., 2014). The "time of challenge (exposure to the virus) after vaccination significantly influences the number of vaccinated animals becoming clinically infected" (Cox et al., 2007). Meaning, a longer period of time between vaccination and virus challenge would likely result in fewer animals showing clinical signs. Most experimental studies focus on cattle that had been vaccinated at least three days prior to challenge with FMDv (Cox & Barnett, 2009). This is in contrast to the scenarios in this document that propose vaccination of infected herds where animals in all stages of the disease would be immunized. This also emphasizes the importance of vaccinating susceptible premises within the control zone prior to moving animals off of infected premises. Identifying the effects of vaccines on the immune responses of actively infected animals should be an area of future research.

Effects of vaccination on viral shedding:

Virus shedding has been shown to be substantially reduced by vaccination with a high-potency vaccine (Bates et al., 2003; Cox et al., 1999; Doel et al., 1994; Salt, Barnett, Dani, & Williams, 1998). Viral RNA has also been found to be, on average, 100 to 1000 times lower (two to three log reduction) in the positive samples of vaccinated animals compared with the unvaccinated animals, suggesting vaccination can help reduce the amount of viral shedding into the environment shortly after direct challenge (Cox et al., 2005). Other findings suggest that vaccination helps to significantly reduce clinical signs in cattle and prevent viremia (Cox et al., 2005; Cox et al., 2007; McVicar & Sutmoller, 1976). Identifying the effects of vaccines on viral shedding in animals that had been exposed to the virus prior to inoculation should be an area for further research.

Effects of vaccination in carrier cattle:

Cox, et al., 2005 showed that 45% of vaccinated cattle can become persistently infected where much of this virus persists within the oropharynx and/or pharyngeal fluid (Garland ARM., 1974). A study by Parida, 2009 states that up to 50% of ruminants can become persistently infected regardless of their vaccination status. However, Doel and Barnett, 1994 showed that there may be a correlation between viral persistence and the time lapse between vaccination and challenge (Doel et al., 1994). Viral persistence may also be influenced by the intensity of the challenge, as well as the type of vaccine itself (Doel et al., 1994).

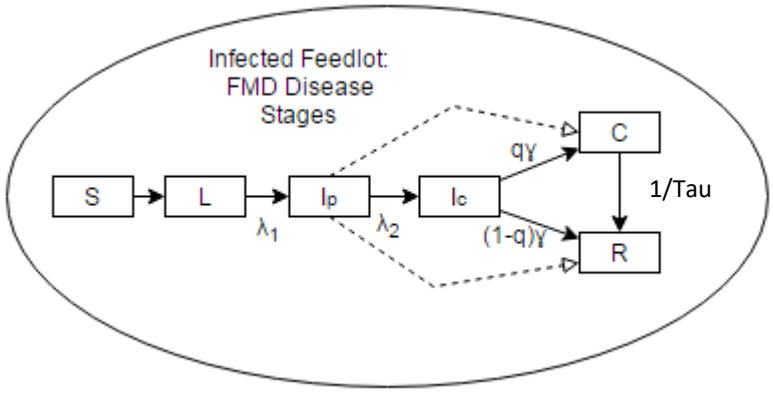
A recently published study by Parthiban., et al, 2015 showed that unvaccinated cattle "excrete significantly higher levels of virus for longer periods of time compared with vaccinated cattle", which could affect the amount of virus found in the environment at the infected or recovered premises (See Table 4). The environmental viral load may also depend on how many animals were able to develop adequate immunity prior to virus exposure.

Table 4: Number of days in which virus is detected in the secretions of vaccinated and non-vaccinated carrier cattle (Parthiban, et al., 2015)

	Carriers (unvaccinated)	Carriers (vaccinated)	Non-carriers (unvaccinated)	Non-carriers (vaccinated)	Units
Nasal fluid	10	4.5	14	2.5	days
Saliva	10	2.3	10	2.5	days

Modeling Overview

A stochastic disease transmission model was applied to simulate the spread of FMDv within a herd and estimate the number of cattle in various disease states at each time period. The disease states include: susceptible (S), preclinically infectious (I_p), clinically infectious (I_C), carriers (C) and fully recovered (R). The main output of the model was to estimate the proportion of cattle in different phases of infection at different points in time for the purpose of identifying the periods of time that would present the highest likelihood of virus transmission when shipping cattle to slaughter.



S = Susceptible
L = Latent
I_p = Pre-clinical
I_C = Clinical
C = Carriers
R = Fully recovered
*Dotted lines were not modeled

Figure 2: Model of progression of FMD through an infected feedlot

The model updates the number of cattle in each disease state every day, which provides insight into the disease progression through the herd. The uncertainties in input variables as well as the inherent variability associated with the course of infection in each animal and the spread within the group are considered in the model.

Parameter distributions for the disease spread model were obtained from previous work by APHIS (USDA, 2012).

Table 5: Input parameters and distributions used in the FMD within-herd model in a beef cattle herd

Variable	Input Distribution/Value
Latent Period (1/ λ1)	Exponential (0.709)
Pre-clinical Period (1/ λ2)	Log normal (0.862, 0.774)
Clinical Period (1/ ɣ)	Gamma (4.752, 0.736)

Carrier Period (1/Tau)	Normal (1095, 180)
q	0.5
Farm Size	10,000 (beef)
Adequate Exposures per time step	Poisson (1.5)

The assumptions applied to the model included the following:

- Transmission occurs
- Pre-clinically and clinically infectious animals are equally infective with respect to transmitting FMD.
- Cows in the susceptible state in a given time period all have an identical probability of becoming infected in the next period (i.e. differences in exposure due to grouping of cows in pens is not considered). This may overestimate the number of adequate exposures in large feedlots.
- Variability in adequate contact due to differences in cow density (number of cows per unit area) is not considered (i.e. transmission is modeled as frequency dependent).
- The probability that a susceptible cow has an adequate exposure with at least one infected cow during a time step is,

$$P_t = 1 - e^{-\frac{k*N_{I,t}}{N-1}}$$

Where *k* is the number of adequate exposures per infected animal, $N_{I,t}$ is the number of infectious animals at time *t*, and *N* is the total population size. This equation assumes that the number of adequate contacts each cow has in a time period is Poisson distributed with mean *k*. The number of susceptible animals that become infected with FMD during each time step is,

$$I_{t,t+1}^{new} \sim Binomial(S, P_t)$$

- Inputs for the analysis are based on published literature and the best current knowledge of the disease biology.

Pathway Analysis

This document is aimed at identifying the main pathways for FMDv spread into susceptible species during the movement of cattle not showing clinical signs from an infected premise. This document does not, however, provide an analysis that determines the amount of risk, and further research in this area is recommended.

In Figure 3, the main release and exposure pathways are identified as follows:

- Pathway 1: Cross-contamination with FMDv during movement due to release of excretions and secretions from viremic non-clinical cattle, and environmental fomites (dirt, bedding, manure, urine) on cattle being moved.
- Pathway 2: Aerosol transmission of FMDv particles from latent, viremic non-clinical, and recovered cattle during transport.
- Pathway 3: Cross-contamination FMDv during movement due to environmental contamination on the method of conveyance.
- Pathway 4: Aerosol transmission of FMDv particles during transport due to environmental contamination on the method of conveyance.

The purpose of this analysis is to identify the different pathways for disease spread, and the effects of vaccination status and timelines. This initial analysis addresses the potential viral pathways associated with moving latent, viremic non-clinical, and recovered cattle from a FMD infected or recovered premises. The likelihood of virus spread will vary depending on the disease phase in which the animal is in and the scenario that is presented.

Vaccination status may have an effect on the likelihood of disease spread, and these potential differences will be addressed in the pathways. Emergency vaccination of cattle has been shown to be effective in preventing or reducing clinical disease and intra-herd transmission and decreasing FMDv shedding. However, the majority of experimental studies were performed in animals that had been vaccinated about 3 days prior to disease exposure or challenge. The scenarios presented in this analysis involve the vaccination of cattle on an infected or recovered premise that have already been exposed to the virus. Based on the current understanding of FMD vaccine implementation and efficacy, the same pathways (see Table 6) will still be addressed in cattle that have been exposed to FMDv prior to vaccination as in those cattle that were never vaccinated. The effect that vaccination has on cattle that have not been exposed to virus is explained below.

Table 6 presents an overview of the pathways evaluated in the present document for the movement of unvaccinated and vaccinated cattle to the harvest site.

Table 6: Potential FMDv pathways associated with the transportation of unvaccinated and vaccinated latent, viremic non-clinical and recovered cattle from infected or recovered farms to slaughter

		Latent Cattle	Viremic non-clinical Cattle	Recovered Cattle
Animal Movement	Pathway 1 (Mechanical Transmission)	Skin Latent -> Pre-clinical Environmental Fomites on cattle (dirt, bedding, manure, urine)	Excretions/Secretions/Skin Environmental Fomites on cattle (dirt, bedding, manure, urine)	Environmental fomites on cattle (dirt, bedding, manure, urine)
	Pathway 2 (Aerosol Transmission)	Aerosol from OP area Aerosol from skin cells Aerosol from fomites on cattle	Aerosol via respiration Aerosol from skin cells Aerosol from fomites on cattle	Aerosol from OP area Aerosol from fomites on cattle
		Conveyance		
Conveyance (Truck) Movement	Pathway 3 (Mechanical Transmission)	Environmental Fomites (dirt, bedding, manure, urine)		
	Pathway 4 (Aerosol Transmission)	Aerosol from fomites on cattle		

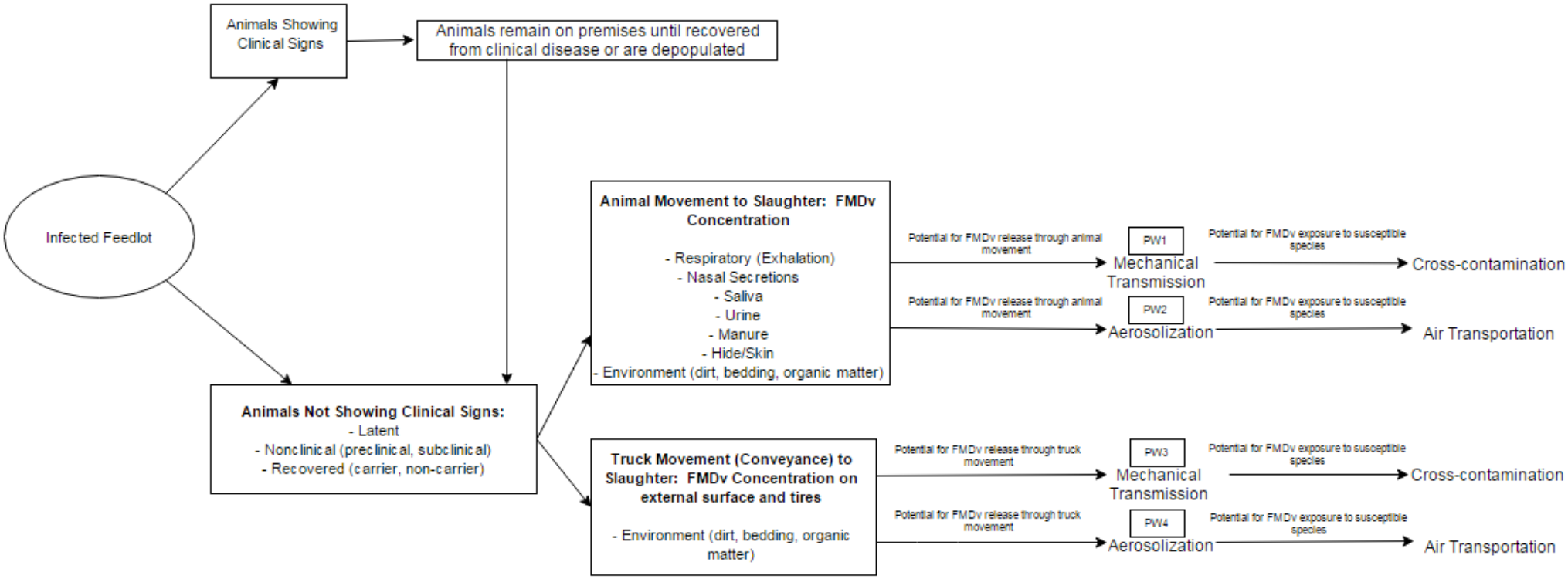


Figure 3: Pathway analysis for moving cattle not showing clinical signs to slaughter

Pathway 1: Cross-contamination with FMDv during movement due to release of excretions and secretions from viremic non-clinical cattle, and environmental fomites (dirt, bedding, manure, urine) on cattle being moved.

Latent cattle: Cattle that are in the latent period have been exposed to virus but virus is not yet detectable in blood. These animals are generally considered not to be infectious and not shedding virus. With that said, virus has been shown to be present in certain skin cells prior to the onset of viremia (the end of the latent period). This potential pathway, however, has never been proven to result in disease transmission during this phase of infection and the likelihood is very low. The pathways associated with moving these cattle would be the following:

Unvaccinated:

- Mechanical transmission from the shedding of skin cells. There has been no evidence of virus transmission due to this route and the likelihood of this happening is very low.
- The disease status of the cattle moves from the latency phase to the pre-clinical phase during transport. Cattle harvest establishments tends to be concentrated around feedlots to allow for easy movement to harvest. USDA states that, on average, cattle are transported 100 miles to harvest (Sheilds & Mathews Jr., 2003) which is equivalent to only about 2 hours of travel time. Due to a relatively short transportation time, it is not likely that cattle in the latent phase would enter the pre-clinical phase during transport and therefore, the associated likelihood of disease transmission from these animals is low.
- Mechanical transmission of virus particles found on the animals. Virus is known to survive for days to months in cold weather. The amount of virus cattle can carry on their hides is unknown and should be an area of further research.

Vaccinated:

- Mechanical transmission from the shedding of skin cells. While there hasn't been a study addressing the effects of vaccination on this particular topic, there is supporting evidence that an effective vaccine can help reduce virus replication which can, in turn, result in decreased viral shedding in cattle. A transmission event is unlikely to occur from this group of animals.
- The disease status of the cattle moves from the latency phase to the pre-clinical phase during transport. Further research is needed to determine the effects of vaccination on the length of the latent period, but the likelihood of disease transmission from these animals is likely low.

- Mechanical transmission of virus particles found on the animals. Vaccines have been shown to decrease FMD viral replication and shedding, which means that vaccinating animals will likely result in less environmental contamination.

Viremic non-clinical cattle: The term viremic non-clinical cattle refers to those animals which are pre-clinical and sub-clinical. During this phase, the animal is viremic, is shedding virus, but has either not yet developed clinical signs (pre-clinical) or won't ever develop clinical signs (sub-clinical). These animals represent the highest likelihood of virus spread because they are actively infectious and can easily go undetected. A study conducted by Rueda, et al., 2014 predicted virus levels to be lower in most secretions from viremic non-clinical cattle when compared with clinical cattle. However, it is still known that disease can occur in this group of animals. Therefore, viremic non-clinical cattle should be treated as if they are secreting a similar amount of virus as clinical cattle, out of an abundance of caution, until further research into this area is done. The pathways associated with moving these cattle would be the following:

Unvaccinated:

- Mechanical transmission from infected excretions/secretions. As stated earlier, cattle that are not showing clinical signs can still shed FMDv. See Table 2 for the predicted virus levels in various bodily fluids. Shedding in viremic non-clinical animals represents an area where further research can be done.
- Mechanical transmission of virus particles found on the animals.

Vaccinated:

- Mechanical transmission from excrertions/secretions. Studies show that FMD vaccines are unable to protect against sub-clinical infection but they may result in decreased viral replication and excretion. Animals that have had time to develop protection following vaccination will shed lower amounts of FMDv and, thus, the event of mechanical transmission from animal secretions will be unlikely. Further research is needed to determine the effect of vaccines on virus shedding in animals that were exposed to the disease prior to vaccination.
- Mechanical transmission of virus particles found on the animals.

***Recovered cattle*:** This term refers to cattle that have recovered from clinical disease. These animals can be split into two groups: a) Carriers; b) Non-carriers. Non-carriers are no longer carrying the virus and are considered to be noninfectious. However, it has been shown that over 50% of cattle can become carriers. Carrier cattle have only been shown to harbor virus in

the oropharyngeal region and research has not demonstrated that carrier cattle are capable of infecting susceptible animals.

Unvaccinated:

- Mechanical transmission of virus particles found on the animals.

Vaccinated:

- Mechanical transmission of virus particles found on the animals. A longer period of time between immunization and virus challenge, results in better protection and a decreased likelihood of becoming persistently infected. It is also important to note that vaccinated cattle have been shown to carry less virus for shorter periods of time than unvaccinated cattle (see Table 4). Recovered cattle pose a lower likelihood of virus transmission than viremic non-clinical cattle and may pose a lower likelihood of virus transmission than non-vaccinated carrier cattle.

Pathway 2: Aerosol transmission of FMDv particles from latent, viremic non-clinical, and recovered cattle during transport.

FMDv has generally been shown to be aerosolized through the respiratory route (exhalation). In cattle, the average amount of virus excreted via the respiratory route has been reported as 4.33 log $TCID_{50}$/mL.

Concern surrounding aerosolization of environmental fomites applies to all latent, viremic non-clinical, and recovered animals that are being moved from infected and recovered premises as FMDv contaminated fecal material can be adhered to the external body surface of the animal. Aerosolization and air movement of aerosolized particles is a rare event that requires adequate particle size and climatological conditions. More research is needed to determine how much risk is associated with virus becoming aerosolized from the environment.

***Latent cattle*:** Animals are not viremic in this phase. However, infectious virus has been found to be present in the oropharyngeal area as early as 2-14 hours after intranasal inoculation and in the interdigital clefts and coronary bands as early as 6 hours after aerosol exposure to FMDv. While the virus has been detected early on, there must be enough virus particles released in order for disease to occur. Therefore, the event of disease spread is very unlikely due to the small quantity of virus intermittently found in this phase. The pathways associated with moving these cattle would be the following:

Unvaccinated:

- Aerosolization of virus particles from the oropharyngeal area. This should be an area for further study.
- Aerosolization of infected skin cells. This should be an area for further study.
- Aerosol transmission of virus particles found on the animals.

Vaccinated:

- Aerosolization of virus particles from the oropharyngeal area. Virus has been shown to be present in the OP region prior to the onset of viremia (the end of the latent period). However, this potential pathway has never been proven to result in infection during this disease phase and disease transmission unlikely. The effects of vaccination on FMDv located in the OP region prior to viremia should be an area for further study.
- Aerosol transmission of virus particles found on the animals. The amount of virus in the environment may be less in a herd that was vaccinated as opposed to an unvaccinated herd. Therefore, the pathway will still be present, but it may be less likely for disease transmission to occur via this route. Further research into the amount of virus present in the environment of a vaccinated herd is needed.

***Viremic non-clinical cattle*:** Viremic non-clinical cattle should be treated as if they are secreting the same amount of virus as clinical cattle out of an abundance of caution, pending results of further research. The pathways associated with moving these cattle would be the following:

Unvaccinated:

- Aerosolization of virus particles from the oropharyngeal area.
- Aerosolization of infected skin cells. A less common route of potential aerosol transmission was proposed in a review by Dillon, 2011. This review discusses the possibility that exfoliated skin cells may also spread disease through aerosolization. Even though the likelihood may be small, the possibility for spread via this pathway must be acknowledged. This group of cattle will pose a higher likelihood of disease transmission due to their ability to shed virus while going undetected.
- Aerosol transmission of virus particles found on the animals.

Vaccinated:

- Aerosolization of virus particles from the oropharyngeal area. Vaccination has generally been shown to decrease the amount of virus that is shed. However, even with vaccination, virus has been shown to persist in the pharynx of inoculated cattle and, thus, there is potential for aerosolization. The likelihood

of disease transmission from these animals, however, may be lower than viremic non-clinical cattle that have not been vaccinated.
- Aerosolization of infected skin cells.
- Aerosol transmission of virus particles found on the animals.

***Recovered cattle*:**

Unvaccinated: The pathways associated with moving these cattle would be:
- Aerosolization of virus particles from the oropharyngeal area. Virus has been shown to persist in the oro-pharynx of carriers for up to three years and it has been shown that disruption (damage) of the cells is often required in order to detect virus. It is, however, highly unlikely the virus can escape and be aerosolized.
- Aerosol transmission of virus particles found on the animals.

Vaccinated:
- Aerosol transmission from the oropharynx. While vaccination has been shown to decrease the amount of virus shed by cattle clinically affected by FMDv, it has not been shown to prevent cattle from entering the carrier state. While there is potential for vaccinated carrier cattle to transmit disease, it is unlikely that this event will occur.
- Aerosol transmission of virus particles found on the animals.

Pathway 3: Cross-contamination of FMDv during movement due to environmental contamination on the method of conveyance.

For the purpose of this analysis, all trailers are assumed to be cleaned and disinfected after each load and unload. This minimizes the amount of fecal material attached to the surface of the trailer. Pathways associated with the movement of a truck and trailer would be:

Unvaccinated:
- Mechanical transmission from dirt, bedding and manure that accumulates outside and inside the vehicle at the infected or recovered premises during loading of animals. For example, high amounts of FMDv can be shed in feces of viremic non-clinical and clinical animals (see Table 2) and also survive in these matrices for a long time. It is, however, unknown the amount of FMDv that can accumulate on and within these methods of conveyance and this requires further research.

Vaccinated:

- Mechanical transmission from dirt, bedding, manure that accumulated on or within the vehicle at the infected or recovered premises during loading. While the pathway is still present, transmission may be less likely to occur in vaccinated animals due to decreased shedding of virus in the environment. However, this should be an area for further research.

Pathway 4: Aerosol transmission of FMDv particles during transport due to environmental contamination on the method of conveyance.

Pathways associated with the movement of a truck and trailer would be:

Unvaccinated:

- Aerosol transmission of virus particles that have been stirred up from the environment. High amounts of virus can be found in fecal material and other animal excretions. Also, the conditions for virus aerosolization are very specific. This event seems to be unlikely to occur. However, more research is needed to determine the risk factors that allow the virus to be aerosolized when attached to the surface of the trailer.

Vaccinated:

- Aerosol transmission of virus particles that have been stirred up from the environment. Vaccinated animals have been shown to shed less virus, and this may result in less virus load in the environment. More research is needed to determine if there is a difference in virus levels in these environments and how much risk is associated with aerosolized virus from the environment these animals live in.

Application of the within herd model to specific scenarios

Five different scenarios were chosen as plausible to occur during a FMD outbreak. In order to estimate the number of cattle in each of the disease phases, a within herd disease spread model was developed and applied to the scenarios. This model used a 10,000 head beef cattle herd to determine the number of cattle in the latent, pre-clinical, clinical, and recovered phases at different times over a time period of 65 days. This time period was chosen based on how long the model predicted it would take for a 10,000 head cattle herd to recover from clinical disease.

Scenario 1: The disease is allowed to progress through an infected herd and at least 42 days have passed since the first observable clinical signs prior to movement of eligible cattle (at or near target weights) to harvest.

Post-infection: Literature shows that cattle will recover from clinical infection after 28 days. At this point, cattle enter the recovered phase, which consists of a population of carriers and non-carriers. Table 7a reflects the spread of disease through a large herd and displays the number of cattle in each disease phase 28 days after the first animal in a 10,000 head beef cattle herd was infected (Day 0 = first day of infection in a herd).

Table 7a: Average number of cattle out of a 10,000 head herd at each disease phase 28 days post-infection

Disease phase	Mean	95% Confidence interval
Susceptible	517	396-638
Latent	123	102-144
Pre-clinically infectious	512	470-554
Clinically infectious	2,851	2,783-2,918
Recovered	3,010	2,943-3,077
Carrier	2,988	2,922-3,054

The results of the model used in this document show that at 28 days post-infection in a 10,000 head herd, 60% of the population (5,998/10,000) will have recovered from the clinical phase of FMD, while approximately 34% (3,363/10,000) will still be shedding virus with 15% (512/3,363) of these infectious animals going undetected due to pre-clinical infection. If a decision is made to move animals not showing clinical signs at this point, a significant proportion of pre-clinical animals (shedding the virus) is predicted to be part of the group moving to harvest.

The time period for moving cattle from the premises to harvest is usually short (a matter of hours). However, there is the possibility that certain animals break with clinical signs before the ante-mortem inspection and the whole group be rejected from being harvested. Also, the

viral load in the environment (fecal shedding and airborne transmission) would still be high, as a significant proportion of animals are actively shedding virus. In addition, knowledge of the time of infection in any herd is almost impossible due to lack of FMD testing protocols, the latent period, and the ability of the disease to remain sub-clinical for a short period of time. Therefore, a more practical approach is to establish a timeline of disease spread based on the first observed clinical signs in a herd.

Post-detection:

Scenario 1 refers to a 42 day post-detection waiting period. This number provided an estimate for the amount of time it would take an individual animal to recover. Therefore, the model was run to provide a more accurate prediction of the time it would take an entire herd to recover.

In a large cattle herd, it is assumed that approximately 10% (1,000 cattle in a 10,000 head herd) of the herd needs to be showing clinical signs before the disease is detected (Bjork et al., 2013). The model used in this document predicted that the time it would take for FMDv to be detected would be approximately 17.5 days (95% CI = 17.4-17.7) post infection. The model results show that 96% (9,628/10,000) of a beef cattle herd of 10,000 head will have entered the recovered phase at 65.7 days post-infection (95% CI = 65.3-65.9) resulting in a viremic population of .009% (.942/10,000). This means the likelihood of disease transmission would be greatly reduced given a 48 day waiting period from the time of detection. Scenario 1 estimates recovery for an individual animal at 42 days. The model results show that waiting an additional 6 days for a large herd would result in a lower likelihood of disease transmission from infected animals (Table 7b).

Table 7b: Average number of cattle out of a 10,000 head herd at each disease phase with waiting periods of 42 days (59 days post-infection) and 48 days post-detection (65 days post-infection)

	Mean (95% Confidence Interval)	
Disease phase	**42 days**	**48 days**
Susceptible	372(255-489)	372(255-489)
Latent	0.19(0.12-0.26)	0
Pre-clinically infectious	1.17(0.68-1.65)	0.002(-.0008-0.005)
Clinically infectious	188(177-199)	0.94(0.86-1.02)
Recovered	4784(4725-4843)	4,980(4,919-5,040)
Carrier	4654(4598-4711)	4,648(4,778-4,835)

The model predicts that approximately 46% (4,980/10,000) of recovered cattle will become carriers and FMDv may persist in the pharynx at the time of transportation and the remainder of the cattle will fully recover with no virus persistence.

Potential Pathways:
Table 7c lists the potential disease pathways that are associated with this scenario. The main pathways would be mechanical transmission of virus from a recovered feedlot and the possibility of aerosol spread of virus from carrier cattle. As stated earlier, there is no evidence to support that carrier cattle are capable of transmitting FMDv to susceptible animals which would indicate that transmission from these animals is not likely. The possibility of virus traveling via environmental fomites from cattle hides or the method of conveyance is possible, but further research needs to be done in this area to quantify the associated risk.

Table 7c: Scenario 1 potential FMDv pathways

Pathway		
Animal Movement	PW1 (Mechanical)	Environmental contamination on animals
	PW2 (Aerosol)	Carrier: Virus from OP area Environmental contamination on animals
Conveyance (Truck) Movement	PW3 (Mechanical)	Environmental contamination on the truck
	PW4 (Aerosol)	Environmental contamination on the truck

Scenario 2: The feedlot is actively infected (animals with clinical signs are present) and cattle not showing clinical signs of FMD (non-infected, latent, viremic non-clinical, recovered) that are eligible for harvest (at or near target weights) are moved to harvest.

While latent and carrier cattle are not known to present a risk for transmission of FMDv, viremic non-clinical (pre-clinical and sub-clinical) animals are known to be a source of virus transmission to susceptible animals. Depending on where the transportation date falls in the progression of the disease through the feedlot, there could be a higher or lower likelihood of disease transmission associated with the movement of the animals (see Table 8a). In addition, a feedlot that is currently infected is likely to contain more virus in the environment, compared to a recovered feedlot, due to the presence of viremic animals that are actively shedding virus. For these reasons, transporting cattle in Scenario 2 will result in a higher likelihood of transmitting FMDv to susceptible animals than transporting cattle in Scenario 1 (unvaccinated cattle - waiting period of 42 days post-detection). Table 8c lists the potential pathways that are associated with each pathway in this scenario.

Table 8a: Average number of cattle out of a 10,000 head herd at each disease phase at 0, 11, 18, 25, 32, and 29 days post-detection

	Mean (95% CI)					
Disease Phase	**0 days**	**11 days**	**18 days**	**25 days**	**32 days**	**39 days**
Susceptible	6,620(6,547-6,694)	517(396-638)	377(260-494)	372(255-489)	372(255-489)	372(255-489)
Latent	1,376(1,319-1,432)	123(102-144)	6.3(2.4-10.2)	0.2(0.1-0.3)	0.03(0.02-0.05)	0.006(0.0005-0.01)
Pre-clinically infectious	1,095(1,064-1,125)	512(470-554)	31(22-39)	1.2(0.7-1.6)	0.1(0.06-0.2)	0.02(0.01-0.03)
Clinically-infectious	692(682-702)	2,851(2,783-2,918)	861(823-900)	188(177-199)	38(36-41)	7.6(7.1-8.1)
Recovered	108(106-111)	3,010(2,943-3,077)	4,397(4,339-4,456)	4,784(4,725-4,843)	4,891(4,831-4,950)	4,937(4,876-4,997)
Carrier	108(106-111)	2,988(2,922-3,054)	4,328(4,271-4,385)	4,654(4,598-4,711)	4,699(4,642-4,757)	4,684(4,627-4,741)

Assuming FMD would be detected at approximately day 17 (Day 0 = day of first infection in herd), a waiting period of 25 days post-detection would result in a reduced likelihood of disease transmission. At this point, approximately .012% (1.2/10,000) of pre-clinical cattle are predicted to be present in the herd and there would be a lower likelihood of moving viremic cattle. Not all cattle will be moved at once, so as the waiting time progresses past the 25 days, the likelihood of transporting a pre-clinical animal decreases, as can be seen in the above table. This number, however, does not include the number of sub-clinical cattle that may be present in the herd and shedding a similar amount of FMDv as clinical cattle. Literature has shown approximately 11% of cattle may remain sub-clinical (Henderson WM., 1985; Sutmoller and Olascoaga, 2002). The model used in this document did not account for sub-clinical cattle and this could be an area for future research.

Table 8b: Scenario 2 potential FMDv pathways

Pathway		
Animal Movement	PW1 (Mechanical)	Latent: Skin, transition to pre-clinical Viremic non-clinical: Excretions/secretions/skin Environmental contamination on animals
	PW2 (Aerosol)	Latent: Virus from OP area, skin Viremic non-clinical: Skin/respiration Carrier: Virus from OP area Environmental contamination from the animal
Conveyance (Truck) Movement	PW3 (Mechanical)	Environmental contamination on the truck
	PW4	Environmental contamination on the truck

	(Aerosol)	

Scenario 3: Upon detection, all cattle in the infected feedlot are vaccinated, at least 42 days have passed since the first observable clinical signs in the herd and cattle eligible for harvest (at or near target weights) are subsequently moved to harvest.

This scenario addresses the pathways associated with transportation of vaccinated carriers. Cattle that were vaccinated prior to exposure have been shown to remain carriers for a shorter period of time and harbor significantly less virus than cattle that were not vaccinated (Parthiban ABR., et al., 2015). It is unknown whether this applies to animals that were vaccinated after exposure to the virus. In this scenario, many of the animals will be vaccinated after exposure which means that there may be more viral shedding and more carriers present than if the animals had been vaccinated prior to exposure.

Scenario 3 is similar to Scenario 1 (unvaccinated cattle - waiting period of 42 days post-detection) in that animals will not be moved until the whole herd is assumed to have reached the "recovered" state. As stated above, the time at which 96% of a 10,000 head beef cattle herd was predicted to be in the recovered phase was approximately 65.7 (95% CI = 65.2-66.1) days post-infection, which means a 48 day waiting period from the time of detection would result in a lower likelihood of moving viremic cattle (Tables 7b). In summary, Scenario 3 results in less likelihood of disease transmission than Scenario 2 (unvaccinated cattle moved prior to herd reaching recovered phase) and a similar or lower likelihood of disease transmission than Scenario 1. The variability in the likelihood of disease transmission in comparison to Scenario 1 exists because of the possibility of lower levels of virus in the environment due to an assumed decrease in viral shedding from vaccinated animals. The identified pathways in this scenario are presented in table 9.

Table 9: Scenario 3 potential FMDv pathways

Pathway		
Animal Movement	PW1 (Mechanical)	Environmental contamination on animals
	PW2 (Aerosol)	Carrier: virus from OP area Environmental contamination from the animal
Conveyance (Truck) Movement	PW3 (Mechanical)	Environmental contamination on the truck
	PW4 (Aerosol)	Environmental contamination on the truck

Scenario 4: Upon detection, all cattle in the infected feedlot are vaccinated, at least 14 days have passed as the waiting period and cattle not showing clinical signs of FMD (non-infected, latent, viremic non-clinical, recovered) that are eligible for harvest (at or near target weights) are moved to harvest.

Cattle that have been vaccinated have been shown to have less severe or no clinical signs, and decreased shedding. There may also be some evidence to indicate fewer of these animals become sub-clinically infected. However, much of this research has been applied to animals that were vaccinated prior to exposure or challenge and it is important to consider the same pathways that were identified for unvaccinated animals leaving an infected or recovered premise because of this unknown. Based on current literature, the number of cattle in each disease phase at these time periods would be very similar to those in Scenario 2 (unvaccinated cattle moved prior to herd reaching recovered phase) (See Table 8a). An exception to this might be the number of cattle that are in the clinical phase as vaccination has been shown to prevent development of clinical disease (this is not addressed in the model that was developed for this report). However, this scenario is different in that vaccination is being applied to all cattle in an infected herd, leaving little to no time for immunity to develop. This brings to question whether a larger proportion of cattle will develop clinical signs than what has been published in literature and could be an area for further research. However, a decrease in viral shedding from this herd may still result in a lower likelihood of disease transmission.

If FMDv was detected on day 17 and cattle were immediately vaccinated, this scenario would mean movement of these animals no sooner than 31 days after initial infection with the 14 day waiting period. Table 10a shows that on day 31, approximately 0.34% (34/10,000) of the herd will be in the latent phase, and approximately 1.59% (159/10,000) of the herd will be in the pre-clinically infectious phase. Should a decision be made to move the eligible cattle as stated in this scenario, a higher likelihood of disease transmission would be present than in Scenarios 1 (unvaccinated cattle – waiting period of 42 days post-detection) and 3 (vaccinated cattle – waiting period of 42 days post-detection) where there would be smaller chance of moving pre-clinical cattle (See Table 8a).

Table 10a: Number of cattle in each disease phase out of a 10,000 head herd at 14 days post-detection

Disease Phase	Mean (95% CI)
Susceptible	317(214-420)
Latent	34(22-46)
Pre-clinically infectious	159(138-179)
Clinically-infectious	1862(1802-1922)
Recovered	3836(3779-3894)

Carrier	3792(3735-3849)

As in other scenarios, the timeline is important and implementation of a vaccination program at various points in the timeline will yield results that could result in different likelihoods of disease transmission. This scenario will result in a higher likelihood of disease transmission than Scenarios 1 and 3 and a similar to or lower likelihood than that of Scenario 2. The additional time that is given for the animals to recover in Scenarios 1 and 3 offers an additional layer of protection. This is because studies show virus to only persist in the oropharyngeal area of cattle after 28 days have passed since the last observable clinical signs. In comparison to Scenario 2, assumptions can only be made as to the effects of the vaccine on animals in an actively infected herd, which could result in fewer clinical cattle and a lower amount of viral shedding. Further research is recommended to quantify whether there is a significant difference in risk between vaccinated and non-vaccinated cattle in an actively infected herd.

Table 10b: Scenario 4 potential FMDv pathways

Pathway		
Animal Movement	PW1 (Mechanical)	Latent: Skin, transition to pre-clinical Viremic non-clinical: Excretions/secretions/skin Environmental contamination on animals
	PW2 (Aerosol)	Latent: Skin, OP area Viremic non-clinical: Skin, respiration Carrier: Virus from OP area Environmental contamination from the animal
Conveyance (Truck) Movement	PW3 (Mechanical)	Environmental contamination on the truck
	PW4 (Aerosol)	Environmental contamination on the truck

Scenario 5: The feedlot is not known to be infected (infected but undetected or negative) and located within a control zone. All animals have been vaccinated and cattle eligible for harvest (at or near target weights) are moved to harvest after the 14 day waiting period.

The main pathways associated with this scenario would be the movement of viremic non-clinical cattle from an infected but undetected premise. As stated above, if the disease is present and not detected until 10% (Day 17) of the herd is affected, FMDv will most likely not be detected in this herd prior to transport, resulting in the movement of infectious animals. Infection can occur any time before or after vaccination. One scenario might assume the initial infection occurred less than 17 days prior to the date of movement, and therefore go undetected. For example, should a decision be made to move animals 14 days after the herd was infected, there is a higher likelihood of transporting a large number of viremic pre-clinical

animals as approximately 3% (343/10,000) of the herd would fall in this category. Table 11a summarizes the number of animals that can be expected to be in each phase during day 14.

If the herd remains uninfected, there would be no risk to nearby susceptible premises during movement of these cattle.

Table 11a: Number of cattle in each disease phase out of a 10,000 head herd at 14 days post-infection

Disease Phase	Mean (95% CI)
Susceptible	8,954(8,886-9,022)
Latent	438(404-471)
Pre-clinically infectious	343(318-368)
Clinically-infectious	204(190-219)
Recovered	31(29-33)
Carrier	31(29-33)

An effective FMD vaccine has been shown to confer protection in 4 days. Had the vaccine been administered prior to infection, it is likely that it would take even longer for the operation to detect clinical signs because of the ability of the vaccine to prevent clinical signs. If the herd is determined to be infected over the course of those 14 days, a large number of animals will be assumed to be viremic non-clinical, but it can also be assumed there will be less virus shedding, fewer viremic non-clinical animals, and a larger proportion of cattle with full protection from immunization than what is observed in Scenarios 3 (vaccinated cattle – waiting period of 42 days post-detection) and 4 (vaccinated cattle – waiting period of 14 days post-immunization). This is because the vaccine has had more time to provide protective immunity in these animals.

Potential pathways remain the same as those in Scenarios 2 (unvaccinated cattle moved prior to herd reaching recovered phase) and 4, with the exception of the presence of carriers. However, there could be a lower likelihood of disease transmission associated with cattle movement in Scenario 5 than in Scenarios 2 and 4 because of the possibility of increased length of time between vaccination and exposure to the virus, therefore, providing protective immunity and decreasing virus shed.

Table 11b: Scenario 5 potential FMDv pathways

Pathway		
Animal Movement	PW1 (Mechanical)	Latent: Skin, transition to pre-clinical Viremic non-clinical: Excretions/secretions/skin Environmental contamination on animals
	PW2	Latent: Skin, OP area

	(Aerosol)	Viremic non-clinical: Respiration, skin cells Environmental contamination from the animal
Conveyance (Truck) Movement	PW3 (Mechanical)	Environmental contamination on the truck
	PW4 (Aerosol)	Environmental contamination on the truck

Conclusions

- Variables that were determined to contribute significantly to disease spread in the scenarios presented in this document were: Mechanism of spread, disease phase, time of movement, and vaccination status.
- Samples from infected animals that were shown to contain the most virus were: Nasal discharge, upper respiratory tract samples, skin, probang samples, airborne excretion.
- Samples from infected animals that were shown to contain the least amount of virus were: Manure and urine.
- Viremic non-clinical (pre-clinical and sub-clinical) cattle were determined to present the highest likelihood of virus transmission to susceptible premises.
- Latent and carrier cattle were determined to present the lowest likelihood of virus transmission to susceptible premises.
- The highest proportion of shedding animals 33% (3,363/10,000) was predicted to be present around 11 days post-detection.
- The lowest proportion of shedding animals 0.009% (0.094/10,000) was predicted to be at 48 days post-detection. Therefore, a 48 day waiting period from the time of detection would significantly reduce the chances of moving a viremic non-clinical animal from a recovered premise.
- Should the decision be made to move animals from an actively infected premise, a waiting period of 25 days post-detection would result in a proportion of 1.89% (189/10,000) shedding animals compared to a waiting period of 14 days post-detection which would result in a proportion of 20% (2,021/10,000) shedding animals.
- Vaccinated animals may be less likely to transmit disease compared with non-vaccinated animals due to decreased shedding. However, this may be affected by the time lapse between immunization and virus challenge, as well as strength of the virus challenge.
- Further research is recommended to better estimate the risk of disease spread associated with each pathway and to be able to provide recommendations for the movement of cattle in these scenarios.

Limitations

- Virus characteristics were described based on the use of experimental work, which used a limited numbers of animals and specific virus strains.
- The scenarios did not account for the time it would take to manufacture, deliver, and administer vaccines following detection of a positive herd.
- The model developed for this report did not include the number of animals that would be in the sub-clinical phase at each time step.
- The model did not account for the differences in virus characteristics.
- The model did not account for the different feedlot set ups or feedlots of different sizes.
- The model assumed all animals had a chance to come into contact with one another and did not account for the possibility of sub-populations within a herd.

Recommendations for further research

1. Identification and quantification of the risk of transmission from a non-vaccinated infected feedlot to nearby susceptible premises.
2. Identification and quantification of the risk of transmission from a vaccinated infected feedlot to nearby susceptible premises.
3. Identification and quantification of differences in shedding between animals that are pre-clinical and animals that remain sub-clinical instead of entering the clinical state.
4. Identification and quantification of the potential risk of associated with FMDv leaving a facility that slaughters infected animals.
5. Quantification of the amount of viral shedding via respiratory exhalation of carrier cattle.
6. Assessing the number of cattle that remain sub-clinical in an affected herd.
7. Assessing the risk for disease transmission due to aerosolization of infected skin cells.
8. Assess the effect of vaccines on virus persistence in the OP region.
9. Identification of the effect of different weather conditions on the amount of infectious virus in the environment of different sized feedlots at various times during disease progression.
10. Quantification of the amount of virus from the environment that can accumulate on an animal at various time intervals.
11. Quantification of the amount of virus from the environment that can accumulate on a cleaned and disinfected truck and trailer in the time it enters the infected and/or recovered property to the time it leaves.
12. Quantification of the amount of virus that can be aerosolized from environmental contamination on animals and methods of conveyance during transport.
13. Quantification of the amount of infectious virus present in the OP region and in the skin cells of the coronary band of cattle at different disease phases.
14. Quantification of the amount of virus shed in various secretions/excretions from viremic non-clinical cattle.
15. Quantification of the amount of virus shed in various excretions/secretions of vaccinated latent, viremic non-clinical, and clinical cattle.
16. Effects of a vaccine on animals in various phases of the disease.
17. Assess the impact of using a non-random within herd spread model.

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Appendix I: Overview of US beef production and movement

US Beef Production

In 2013, the US ranked as the world's fourth largest global beef producer with beef exports valued at $5.722 billion. This value increased to $6.520 billion in 2014. In 2012, it was estimated that the number of all US cattle and calf operations was 915,000 and the majority of the beef operations (approximately 742,000 in 2010) could be found in Texas, Oklahoma, Missouri, Nebraska and South Dakota. As of July 2015, the total US cattle inventory was estimated at a total of 98.4 million head of which approximately 30.5 million are beef cattle. The beef industry specifically, consisted of 4.90 million beef replacement heifers, 30.5 million beef cows and a calf crop of 34.3 million. Cattle and calves at feedlots for the slaughter market totaled 12.1 million head. Feedlots with 1,000 or more head accounted for 85% of total cattle on feed in July 2015 (FAO, 2015; USDA ERS, 2015; USDA NASS, 2015). According to USDA NASS, 742,000 beef operations were recorded to exist in the US in 2010 with approximately 77,140 of these being feedlots (see Figure 4). This number has declined gradually since 1996 at about 1 to 2% each year. The decrease, however, has been seen primarily in small operations (1 to 49 head). As small operations decrease, large operations (100 or more head) continue to get larger. Today, large feedlots account for over 80% of all cattle that are on feed (See Table 12).

Table 1. Cattle on Feed: Number of Feedlot Operations, Inventory, and Marketed by Feedlot Capacity, U.S., 2010

Feedlot Capacity	*Number of Lots*	*Inventory (x 1,000 head)*	*Percent of Total Inventory*	*Cattle Marketed (x 1,000 Head)*
< 1,000 head	75,000	2,509	17.9%	4,032
1,000 - 1,999	790	454	3.2%	778
2,000 - 3,999	560	800	5.7%	1,400
4,000 - 7,999	335	1,030	7.3%	1,760
8,000 - 15,999	180	1,250	8.9%	2,470
16,000 - 23,999	85	1,130	8.1%	2,040
24,000 - 31,999	55	1,050	7.5%	2,050
32,000 - 49,999	71	2,050	14.6%	4,110
50,000 and Over	64	3,750	26.7%	7,470
All Feedlots	77,140	14,023	100.0%	26,110

Source: National Agricultural Statistics Service, Agriculture Statistics Board, U.S. Department of Agriculture, Cattle on Feed, February 2011, Accessed May 9, 2011 at *http://usda.mannlib.cornell.edu/usda/nass/CattOnFe//2010s/2011/CattOnFe-02-18-2011.pdf*

Figure 4: Cattle on Feed, 2010

(SOURCE: FAD PReP Beef Feedlot Industry Manual 2011, pg. 2 (USDA APHIS, 2011))

Table 12: U.S. Cattle Inventory, 2015 ((USDA NASS, 2015)**)**

Group	No. of Head
All cattle and calves	98.4 million

Beef cows and heifers that calved	30.5 million
Beef replacement heifers	4.90 million
Cattle and calves on feed	12.1 million

The US beef industry is divided into two main production sectors and an intermediate sector that are distributed throughout the US: cow-calf operations, backgrounding, and cattle feeding (USDA, 2012).

Cow-calf operations: While these operations are located throughout the US, there are clusters in the Southeast US, Southern Plains and Mountain Regions (See Figure 5). These herds depend heavily on range and pasture forage conditions as they live primarily off of forage from the pastures with little, if any grain. The calf is maintained on pasture with the cow until it is weaned, at which point it is moved to a feedlot. The average beef cow herd is 40 head, but about 9% of beef operations have 100 or more beef cows.

Backgrounding (Stocking): Younger or lighter-weight calves may be sent to a backgrounder where they are given additional time to gain weight. This stage begins when a calf is weaned and ends when the animal is placed in a feedlot and relies heavily on pasture combined with grain to increase the calf's weight prior to entering a feedlot.

Cattle feedlots: While many of these operations are located in the Great Plains, they are also located in parts of the Corn Belt, Southwest, and Pacific Northwest (See Figure 6). This data is from the most recent census which was in 2002. The purpose of moving cattle to these feedlots is to put them in an environment that is conducive to weight gain. Feeder cattle are typically kept at feedlots for 160 days (Personal communication Robert De Otte Jr.), but this can range from 90 to 300 days depending on desired finish, feeding conditions and other variables. For the purpose of this analysis, a 10,000 head feedlot is used. In general, there are six feedlot facility types (USDA APHIS, 2011):

1. Earthen lot with or without mounds
2. Earthen lot with a windbreak or shed
3. Earthen lot without a windbreak or shed
4. Concrete lot with a shed
5. Complete confinement building with solid floor (concrete or earthen)
6. Complete confinement building with slotted floor.

When it comes to land, feedlots should be hard surfaced, but manure and mud in feedlots can become a problem when there are lower evaporation rates in the winter and/or improper drainage conditions. If prevention measures are unsuccessful, farmers provide mounds of soil and/or additional bedding, such as corn husks or straw to improve conditions (Pohl, 2002).

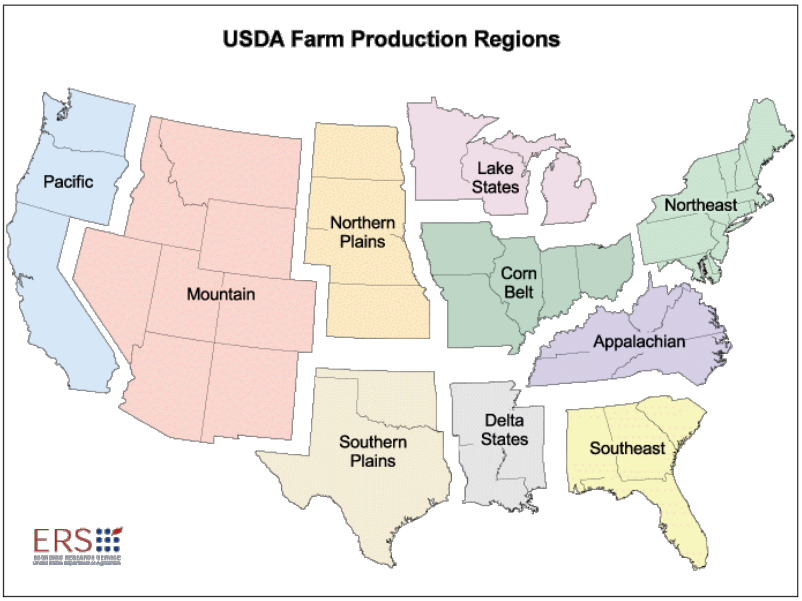

Figure 5: USDA ERS Farm Production Regions
(SOURCE: USDA ERS)

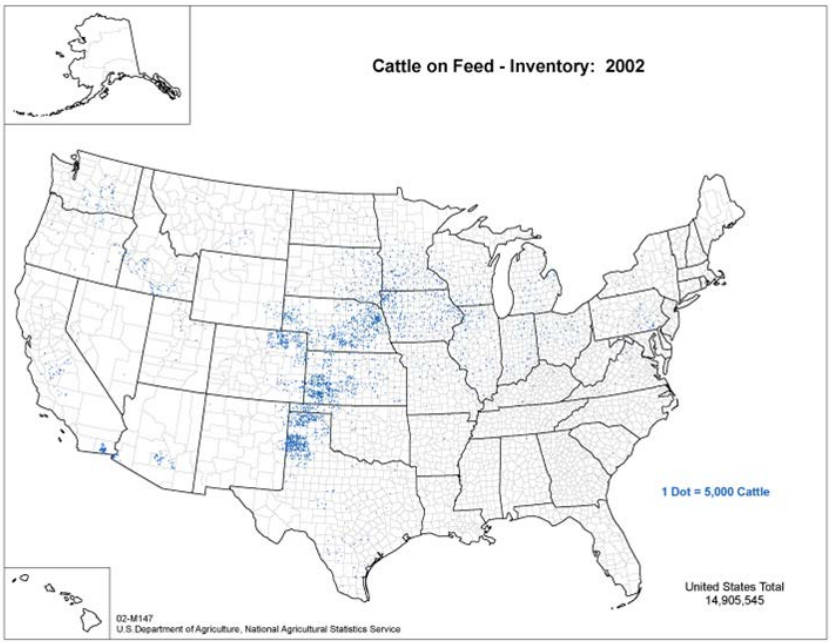

Figure 6: USDA Cattle on Feed
(SOURCE: (USDA, 2002))

Beef Cattle Movement Flows

Cattle movements occur throughout the US and the largest volume tends to be into and within the Northern and Southern Plains (Sheilds & Mathews Jr., 2003), as can be seen in Figure 7. It is important to note that much of the data on cattle movement is based on Interstate Certificate of Veterinary Inspection (ICVI) documentation which is required for the movement of all livestock across state lines except for those that are destined for slaughter (USDA APHIS, 2013). So, while this information can provide insight into where a large proportion of cattle are located and where they move, it doesn't account for the movements of cattle from feedlots to slaughter, which is the focus of this analysis. Shipping distance varies depending on the location of the feedlot and where the cattle are marketed. When it comes to moving feedlot cattle to slaughter, on average, they are shipped approximately 100 miles. Cattle slaughter tends to be concentrated, with more than two-thirds of the operations occurring in the same states as many of the feedlot operations (Sheilds & Mathews Jr., 2003).

Movement Restrictions

It is important to note that in the event of an FMD outbreak, vaccinated animals without clinical signs will not be allowed to move until 14 days post-vaccination (USDA APHIS, 2014).

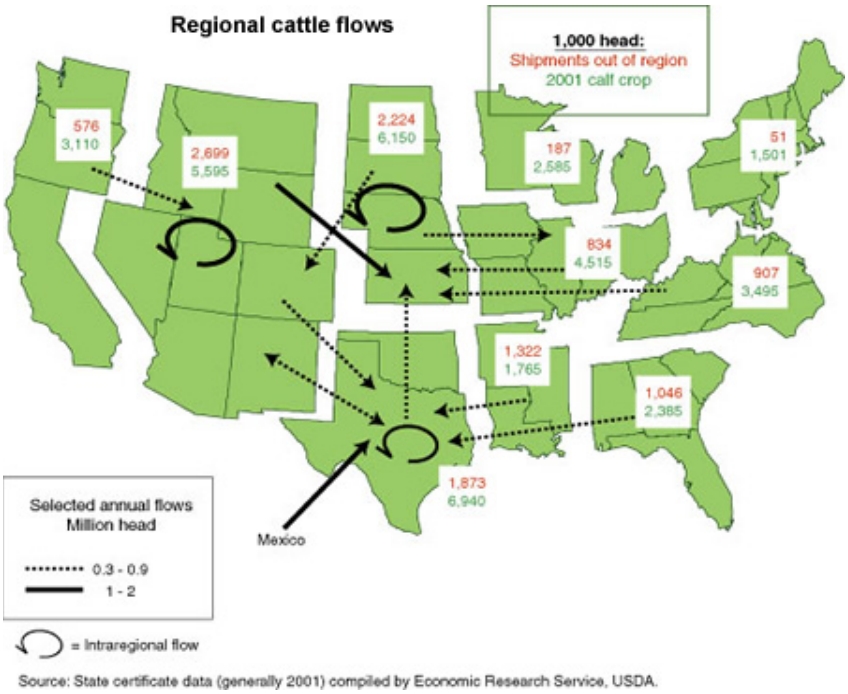

Figure 7: Region cattle flows as depicted by USDA ERS

(SOURCE: (Sheilds & Mathews Jr., 2003))

Beef Cattle Transportation Characteristics

The mode of transportation evaluated for the movement of cattle from an FMD-infected feedlot to a slaughter establishment is a trailer. Low stock trailers (goosenecks) are used to transport smaller numbers of cattle (Figures 8A and 8B). Stock trailers range from 16' 'to 40'. A semi or "pot" trailer is more commonly used as they are able to transport larger groups of cattle over a longer distance (Figures 9A and 9B) (USDA APHIS, 2011). These trailers can range from 34' to 53' feet. Trailers are required to be well-ventilated to protect animals from accumulation of exhaust fumes from other vehicles, excessive heat, high humidity and accumulation of ammonia from urine (Chambers & Grandin, 2001). Non-slip floors are recommended in all trailers to prevent animals from losing their footing. This can be done by using a cross slating grid made from metal or wood or by putting grass or sawdust on the floor of the trailer (Chambers & Grandin, 2001). While full ventilation is required in warm weather, it is recommended to cover one-third to one-half of the holes with plastic panels in a semi-trailer in cold weather to keep cattle at a comfortable temperature during movement (Grandin, 2007).

Figure 8A and 8B : Gooseneck low stock trailer (Exterior and Interior)

Figures 9A and 9B: Semi trailer (Exterior and Interior)

(SOURCES: 8A) Fthr.com; 8B) Swamericana.wordpress.com; 9A and 9B) Feedyardfoodie.wordpress.com)

Transporting animals in a humane manner means providing enough space for each animal to remain comfortable over a long distance. Figure 10 provides recommendations for the number of cattle to be transported based on cattle weight and stock trailer size. Large feedlots tend to use semi-trailers for transporting cattle to slaughter. For semi-trailers the FAO recommends 1.0 to 1.4 m^2 of floor area per animal, and limits are based on total weight and the number of axels. In the U.S. it is common to ship loads that are approximately 48,000 to 50,000 lbs, which is approximately 30 to 42 cattle, with the average typically being 35 or fewer head (Personal communication: Timothy Goldsmith, Robert De Otte Jr.).

Table 3. Guidelines for Cattle Weight on Semi-Trailers for Over-the-Road Transport

Compartment Weight (lbs.)	*Average Weight of Cattle (lbs.)*											
	400	*500*	*600*	*700*	*800*	*900*	*1,000*	*1,100*	*1,200*	*1,300*	*1,400*	*1,500*
1,500	3	3	2	2	1	1	1	1	1	1	1	1
4,000	10	8	6	5	5	4	4	3	3	3	2	2
4,500	11	9	7	6	5	4	4	3	3	3	2	2
6,000	15	12	10	8	7	6	6	5	5	4	4	4
8,000	20	16	13	11	10	8	8	7	6	6	5	5
9,000	22	18	15	12	11	10	9	8	7	6	6	6
20,000	50	40	33	28	25	22	20	18	16	15	14	13
21,000	52	42	35	30	26	23	21	19	17	16	15	14

Source: Loading Suggestions in Master Cattle Transporter Guide, National Beef Quality Assurance Guide for Cattle Transporters, 2007.

Figure 10: Cattle Transport Guidelines
(SOURCE: (USDA APHIS, 2011))

Transportation Regulations

Transportation regulations require that cattle are not confined in a vehicle for longer than 28 consecutive hours unless there are accidental or unavoidable or when the owner has requested that the 28 hour period be extended to no more than 36 hours. If permission for one of these exemptions is not granted, cattle are to be unloaded, fed, watered and allowed to rest for no less than 5 consecutive hours (U.S. Code 2011, Title 49 Chapter 805, Section 80502).